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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Appukuttan & Stout	§	**ART UNIT: 1636**
	§	
FILED: December 19, 2001	§	**EXAMINER:**
	§	**Kaushal, Sumesh**
SERIAL NO.: 10/025,264	§	
	§	
FOR: Lentiviral Vector-Mediated Gene Transfer And Uses Thereof	§	**DOCKET: D6124**
	§	

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Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313

DECLARATION UNDER 37 C.F.R. § 1.132

Dear Sir:

I, J. Timothy Stout, do hereby state as follows:

I am a co-inventor of the above-referenced patent application. I have read U.S. patent application serial no. 10/025,264 and I am aware of the content of the Office Action, including all prior art cited against the '264 application.

An issue relating to the patentability of a method of inhibiting intraocular neovascularization by administering to the eye a lentiviral vector encoding a Mig/IP10 fusion protein is the degree of enablement provided by Applicant's specification. The following data are presented as evidences of enablement commensurate with the scope of the claims:

To demonstrate that administering the lentiviral vector of the present invention to the eye would result in inhibition of intraocular neovascularization, lentiviral vectors encoding an anti-angiogenic molecule, a gene product encoding the 5 kringle domains of the plasminogen protein, were injected into the subretinal space of 12 primates. All primates received subretinal injections in the right eye only. Two weeks following this injection, both left and right eyes of all primates were lasered in such a fashion as to induce subretinal neovascularization akin to that seen with age-related macular degeneration (Fig. 1). Animals were followed weekly or bi-weekly for six months by ophthalmic examination and fluorescein angiography to measure the development of subretinal neovascularization in both eyes. The extent of subretinal neovascularization was graded weekly on a three-point scale (Fig. 2). No difference in the amount, time of onset or severity of neovascularization was seen between the right and left eyes of animals that received control subretinal injections (saline or lentiviral vector encoding the enhanced green fluorescence protein marker gene). Marked inhibition of the size, severity and time of onset of subretinal neovascularization were seen in the right eyes of animals treated with the therapeutic lentiviral vector (Figs. 3-5). Multifocal electroretinography was performed on both eyes of all animals and demonstrated no toxic effect from the surgery or lentiviral vector expression (Fig. 6). Persistence of the anti-neovascular effect was demonstrated by re-lasering the same animals, in the same way, 6 months after the first experiment (Fig. 7). Again, marked inhibition of neovascularization was noted in the right eye of the animals that had received the therapeutic lentiviral vector (Fig. 8).

These data showed that intraocular neovascularization can be inhibited by administering to the eye a lentiviral vector encoding an anti-angiogenic molecule. Based on the data contained herein, I respectfully submit that the scope of the claims 5 and 10 in the '264 application has a reasonable correlation to the scope of the enablement provided.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or patent issued thereon.

Date: 2/15/04

Dr. J. Timothy Stout